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ANGELL, JON E				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

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PATDOCTC@fr.com

# Office Action Summary

**Application No.**

10/535,472

**Applicant(s)**

CHRISTENSEN ET AL.

**Examiner**

J. E. ANGELL

**Art Unit**

1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 22 June 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 43-47, 54-60, 62, 65-67 and 69-72 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 43-47, 54-60, 62, 65-67 and 69-72 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

This Action is in response to the amendment to the claims filed on 6/22/2009, which has been entered.

1. Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claims 43-47, 54-60, 62, 65-67, 69-72 are currently pending and addressed herein.

#### ***Claim Rejections - 35 USC § 112***

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 69, 70 and 72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are indefinite because they depend on claim 68 which has been cancelled.

#### ***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 43-47, 54-60, 62, 65-67, 69-72 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

MPEP §2163.06 notes:

*If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981).*

MPEP §2163.02 teaches that:

*Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application.*

MPEP §2163.06 further notes:

*When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure.*

In the instant case, claim 43 has been amended to require that A and C consist of “between 2 and 5 nucleotide units” and to require that B “consists of between 5 and 10 nucleotide units.” Applicants refer to pages 8-9 of the published PCT priority document for support. However, pages 8 and 9 do not appear to have support for the new limitations. Specifically, pages 8-9 only appear to generally describe that:

A has a length of 2-10 (preferably 2-8, such as 3, 4, 5, 6, 7) nucleotide subunits; B has a length of 1-10 (preferably 5-8, such as 6 or 7) nucleotide units; and C (if present) has a length of 2-10 (preferably 2-8, such as 3, 4, 5, 6, 7) nucleotide subunits...

This does not provide support for the new limitations in the claims. For instance, the new limitations require that B must consist of between 5 and 10 nucleotides units. However, this specific limitation is not found in the specification, including the pages referred to by Applicant. That is, the specification generally sets describes the length of each region, including B, but does not explicitly set forth the specific limitations that are now required.

Furthermore, the claims have been amended to require that one or both of A and C must comprise at least 2 consecutive locked nucleotide units. Applicant refers to page 7, lines 5-11 and 15-21 for support. However, the passages which Applicant refer to appear to indicate that when at least one of the two consecutive locked nucleotide units is an alpha-L-oxy-LNA unit. The amended claims do not include the requirement that at least one of the two consecutive locked nucleotide units is an alpha-L-oxy-LNA unit. Therefore, the amended claim is broader in scope than the specification. It is noted that all claims depend on claim 43; therefore, all claims are included in the rejection.

### ***Non-Statutory Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 43-47, 54-60, 62, 65-67, 71 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-26 over U.S. Patent 7,687,617, which recently issued from Application No. 10/717,434 (previously cited in provisional obvious-type double patenting rejection).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the ‘617 patent are drawn to an oligonucleotide having the formula A-B-C-D, wherein A represents a sequence of locked nucleotide units; B represents a sequence of non-locked nucleotide units, wherein B has a length of 4-20 nucleotide units; C represents a sequence of locked nucleotide units; and D represents a non-locked nucleotide unit or a sequence of non-locked nucleotide units. In certain embodiments the LNAs of A and C may

be beta-D-oxy-LNA units; the oligo may contain phosphorothioate linkages; and B represents a sequence able to recruit RNase H.

Therefore, one of ordinary skill in the art would conclude that the invention defined in the claims at issue is anticipated by, or would have been an obvious variation of, the invention defined in the claims of the '617 patent.

### *Claim Rejections - 35 USC § 103*

6. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 43-47, 54-60, 62, and 65-67, 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kurreck et al. (2002) *Nucleic Acids Res.* 30:1911-1918 in view of:

1. Keinicke et al. (2002) "Alpha-L-RNA (alpha-L-ribo configured RNA): synthesis and RNA-selective hybridization of alpha-L-RNA/alpha-L-LNA chimera"  
*Bioorganic & Medicinal Chemistry Lett.* 12:593-596;

2. Sorensen et al. (2002) "Alpha-L-ribo-configured locked nucleic acid (alpha-L-LNA): synthesis and properties" *J. Am. Chem. Soc.* 124:2164-2176;
3. Orum et al. (WO 01/48190 A2) "Therapeutic uses of LNA-modified oligonucleotides";
4. Wahlestedt et al. (2000) "Potent and nontoxic antisense oligonucleotides containing locked nucleic acids" *Proc. Natl. Acad. Sci.* 97:5633-5638; and
5. Monia et al. (US Patent 6,884,787).  
(All references are previously of record)

The instant claims read on LNA-DNA-LNA gapmers, mixmers, and chimeras comprising one or more alpha-L-oxy LNA nucleotides. The claims embrace compounds and compositions for in vitro or in vivo uses.

As previously indicated, Kurreck et al. taught LNA/DNA mixmers, gapmers, and end blocks, 18-nucleotides in length, capable of inducing RNase H-mediated cleavage of a complementary mRNA target (Table 1, page 1912; and pp. 1913-4). More specifically, Kurreck et al. taught 18-nucleotide LNA-DNA-LNA mixmers, gapmers, and end blocks, having first and second regions (A and C) of at least 1 to 5 oxy LNA monomers in the beta configuration flanking a third, or central, region (B) consisting of DNA and optionally 1 or 2 LNAs (see Table 1). The central DNA gap, which in certain embodiments has at least one LNA, is said to be necessary for recruitment of RNase H (page 1913-4 and 1916-7). In fact, with the exception of LNA 21, each of the oligos disclosed in Table 1 therein has RNase H-mediated mRNA cleavage activity.



Kurreck et al. do not teach alpha-L-oxy LNA nucleotides, or oligonucleotides containing this particular configuration. Further, Kurreck et al. do not teach LNA/DNA oligonucleotides containing phosphorothioate linkages, or compositions comprising oligos and chemotherapeutic compounds. Kurreck et al. further do not teach LNA-DNA-LNA gapmers 16 nucleotides in length.

However, the prior art is replete with disclosures teaching methods and materials for making and using RNase H active, alpha-L-oxy LNA-containing, phosphorothioate oligonucleotides.

For example, Keinicke et al. taught the synthesis and incorporation of  $\alpha$ -L-LNA ( $\alpha$ -L-ribo configuration) nucleotides into short oligonucleotides (pp. 593-596). Testing several LNA/RNA and LNA/DNA mixmers (Table 2), Keinicke et al. showed and taught that the incorporation of three  $\alpha$ -L LNA monomers into a DNA oligonucleotide significantly improves the thermal stability towards both DNA and RNA as compared to standard DNA oligos. It is further shown that  $\alpha$ -L-LNA-containing oligonucleotides display improved hybridization properties to RNAs as well as satisfactory discriminatory behavior (page 595). In addition, Keinicke et al. taught that  $\alpha$ -L-LNAs confer enhanced stability to nuclease digestion as compared to an all DNA oligonucleotide (page 595). In concluding, Keinicke et al. state that their results suggest further studies to evaluate the full potential of the  $\alpha$ -L-LNA oligos as antisense oligonucleotides, suggesting that in general the  $\alpha$ -L-LNA oligos might be expected to have reduced toxicity and improved specificity as compared to current antisense molecules.

Sorensen et al. taught and showed that  $\alpha$ -L-LNA/DNA mixmers are capable of recognizing complementary RNA targets with high specificity, and are resistant to nuclease

degradation. Sorensen et al. further show that  $\alpha$ -L-LNA-containing oligonucleotides are capable of triggering RNase H mediated degradation of a complementary RNA target, and further suggest using such oligos in a steric blocking capacity, thereby recommending their use as antisense oligonucleotides (pp. 2169-2171).

Orum et al. taught methods for making and using phosphorothioated,  $\alpha$ -L-oxy-LNA-containing antisense oligonucleotides and pharmaceutical compositions thereof for inhibiting the expression of a gene in a cell in vitro and in vivo. It is said the LNA oligonucleotides may be used in combination with chemotherapeutic drugs (pp. 9-11, 17, 28-29, see also 1-43).

Wahlstedt et al., cited by Applicant in the Remarks filed 10/30/2008, traversing the enablement rejection, is said to show that one of skill would reasonably expect many different types of antisense oligonucleotides to be capable of inhibiting the expression of a gene. Applicant states Wahlstedt et al. conducted studies using a 15 residue oligonucleotide targeted to the rat 6-opioid receptor. The oligonucleotide consisted of 4 LNA residues followed by 6 DNA residues and then 5 LNA residues (DOR-AS-1 LNA/DNA/LNA gap-mer). The oligonucleotide was injected into the cerebrospinal fluid of rats. The treatment knocked down expression of DORY a G-protein coupled receptor and altered the response of the mice to pain in the presence of an opiate. Thus, the DOR-AS-1 LNA/DNA/LNA gap-mer had a marked en vivo effect. Thus, oligonucleotides can reach targets en vivo and **exert** a physiological effect. Wahlestedt et al. conclude that the tested oligonucleotides containing DNA and LNA exhibited "(i) biological stability, (ii) RNase H activation, (iii) lack of toxicity, and (iv) potent biological activities." Applicant states, while Wahlstedt et al. do not exemplify  $\alpha$ -L-oxy-LNA-containing

oligonucleotides, this is no reason to doubt the oligos of the instant claims would likewise be effective in vivo.

Furthermore, the prior art is replete with disclosures teaching and recommending the use of antisense chimeras or gapmers of various lengths, comprising a central DNA gap flanked by one or more modified or non-standard nucleotides and one or more phosphorothiates to protect the antisense oligonucleotide against nuclease degradation while preserving RNaseH activity. It is clear from the prior art that it was well known at the time of invention that LNAs, 2'-sugar modifications, and phosphorothioates could be used alone and in combination to optimize the stability, solubility, cellular uptake, and activity of antisense oligonucleotide.

Thus, with regard to claims 65-67, in addition to the disclosure of Kurreck et al. teaching the benefits and utilities of LNA-DNA-LNA gapmers, Monia et al. taught that antisense oligonucleotides may be synthesized as composite structures of two or more modified oligonucleotides and/or oligonucleotide mimetics wherein the arrangement of said nucleotides is in the form referred to in the art as "gapmers" (col. 12). It is taught that preferred modifications include phosphorothioate linkages, locked nucleic acids, and 2'-sugar modifications (cols. 8-9). It is taught that these modifications may be combined and incorporated into the same antisense compound to optimize its activity (col. 12, lines 23-35). With regard to claims 59 and 60, Monia et al. taught that antisense compounds can be anywhere from 8 to 50 nucleotides in length, preferably 12-30 nucleotides in length. Thus, for example, an oligo may be 12, 13, 14, 15, or 16 nucleotides in length

Methods and materials for making LNA-containing oligonucleotides were well known in the prior art, as evidenced by Kurreck et al., Monia et al. (col. 9, citing prior art, and col. 12, bottom bridging to 13), Keinicke et al., Sorensen et al., and Orum et al.

Thus, with regard to claims 59 and 60, absent evidence of secondary considerations, the particular length of the antisense oligonucleotide does not patentably distinguish the claimed invention from the prior art, since one of skill would reasonably anticipate LNA-DNA-LNA gapmers and chimeras of lengths in the range disclosed by the prior art to have the same general properties, varying in degree only and not in kind.

Orum et al. (page 28) and Monia et al. taught that antisense oligonucleotides, including chimeras and gapmers, may be formulated in pharmaceutical compositions with one or more chemotherapeutic agents (col. 28, lines 1-10).

Accordingly, the prior art is replete with disclosure teaching and recommending the use of LNA/DNA gapmers and chimeras of the type now claimed, as well as countless other varieties in antisense oligonucleotides of various lengths from about 8 to 50 bases. The benefits and utilities of such LNA-containing compounds is clearly set forth in the prior art, as represented by the references cited herein. Methods and materials for making and using a variety of LNA-DNA-LNA gapmers were widely available, and the level of skill in the art for making and testing such constructs was high. Several exemplary embodiments were available in the prior art, teaching and recommending the use of LNA/DNA gapmers and mixmers of both the  $\alpha$  and  $\beta$  configurations. The combination of prior art as a whole cited herein clearly show that multiple sugar-phosphate backbone modifications may be incorporated into the end-flanking regions as well as the central region of an oligo to improve its properties. Thus, one of skill would have had

a reasonable expectation of success and ample reason to make and use LNA/DNA compositions of the type now claimed.

Accordingly, in the absent of convincing evidence to the contrary, the instantly claimed invention would have been *prima facie* obvious to one of skill in the art at the time the invention was made.

### ***Response to Applicants' Arguments***

8. Applicant's arguments filed 6/22/2009 have been fully considered but they are not persuasive.
9. Regarding the Obvious-type Double Patenting rejection, Applicants state that the rejection will be addressed upon notification of allowable claims.
10. Regarding the 103 rejection, Applicant argues that one would not include alpha-L-oxo LNA in the DNA gap of a gapmer because LNA decrease RNaseH mediated cleavage when included in the gap and that it is surprising that inclusion of alpha-L-oxo LNA in the DNA gap does not decrease the effectiveness of the oligonucleotide as an antisense oligonucleotide. This is not persuasive because the claims do not particularly require that an alpha-L-oxo LNA interrupts a DNA stretch in a gapmer. That is, the claims indicate that A and C consist of between 2-5 nucleotide units wherein all 5 nucleotide units can be locked nucleotide units, and B consists of between 5-10 nucleotide units wherein at least one nucleotide unit is an alpha-L-oxo LNA nucleotide unit, without any requirement where within B the alpha-L-oxo LNA is located. As such, regions A and C could consist of 5 alpha-L-oxo LNAs and B could have one alpha-L-oxo at either end and directly adjacent to the alpha-L-oxo LNAs of A and C regions. Thus, as

currently written, the claims do not require that an alpha-L-oxo LNA interrupts a DNA stretch in the gap of a gapmer.

Applicant argues that one would not substitute alpha-L-oxo LNA for beta-D-oxo LNA in the oligonucleotides of the cited references because, according to Keinicke, alpha-L-oxo LNA have reduced affinity for RNA compared to beta-D-oxo LNA. Applicant also refers to Sorenson's teaching that alpha-L-oxo LNA are not compatible with efficient RNase-H mediated cleavage and Wahlestedt's teaching that miximer LNA/DNA is much less effective than LNA/DNA gapmers in recruiting RNaseH.

In response, it is respectfully pointed out that one of skill in the art would understand that antisense oligonucleotides (AONs) basically have two modes of action which both involve hybridization to the RNA target: steric blocking of the mRNA and recognition of the RNA-AON duplex as a substrate for RNaseH cleavage (e.g., see Sorenson page 2171, last paragraph). The prior art specifically teaches that the addition of alpha-L-oxo LNA monomers into an antisense DNA oligonucleotide would significantly improve the thermal stability towards both DNA and RNA as compared to standard DNA oligos and confer enhanced stability to nuclease digestion as compared to an all DNA oligonucleotide (See Keinicke and Sorenson, as indicated above). Considering that the prior art teaches that inclusion of alpha-L-oxo LNA monomers significantly improves the thermal stability and enhanced resistance to nuclease digestion of antisense oligonucleotides, one of ordinary skill in the art would have had a reason to use alpha-L-oxo LNA monomers in antisense oligonucleotides. Furthermore, the prior art does teach that the alpha-L-oxo LNA oligonucleotides would confer RNaseH cleavage, albeit possibly at a reduced efficiency. Considering the other advantages of including alpha-L-oxo monomers in the

oligonucleotides, which one of skill in the art would recognize as increasing steric blocking of the mRNA, the possible decrease in RNaseH cleavage efficiency would not convince one against including alpha-L-oxy LNA monomers in antisense oligonucleotides. In other words, one of skill in the art, weighing the possible pros and cons recognized in the prior art, would be motivated to include alpha-L-oxy LNA monomers in antisense oligonucleotides and would have a reasonable expectation that inclusion of the alpha-L-oxy monomers would result in antisense oligonucleotides that inhibits expression of a target mRNA.

Furthermore, regarding Applicant's arguments against Wahlstedt, it is respectfully pointed out that Applicant cited Wahlstedt in response to an enablement rejection stating that while Wahlstedt et al. do not exemplify  $\alpha$ -L-oxy-LNA-containing oligonucleotides, there is no reason to doubt the oligos would likewise be effective in vivo.

Therefore, Applicant's arguments are not persuasive.

### ***Conclusion***

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. E. ANGELL whose telephone number is 571-272-0756. The examiner can normally be reached on Monday-Thursday 7:00 a.m.-5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Heather Calamita can be reached on 571-272-2876. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. E. ANGELL/  
Primary Examiner, Art Unit 1635